

REMARKS

As noted previously, this Supplemental Amendment is being filed in response to the Office Communication mailed from the U.S. Patent and Trademark Office on July 26, 2004, in the above-identified application. In that Office Communication, the Examiner stated that the Amendment to the claims filed on 06/09/04 does not comply with the requirements of 37 C.F.R. 1.121(c). This Supplemental Amendment is essentially a re-submission of a Response to an Office Action filed on June 9, 2004, with amendments to the Listing of the Claims in order to comply with 37 C.F.R. 1.121(c). Reconsideration and further examination are requested.

Objections to the Specification

The disclosure was objected to for the following error in the description of the drawings: Figures 23-32 are not properly identified in the specification. The Examiner states that figures appearing in more than one panel must be identified as such in The Brief Description of the Drawings.

Applicant has amended the Specification to identify and describe each panel as they appear in Figures 23 – 32. The Brief Descriptions of the Drawings now properly identify the panels. As such, Applicant respectfully requests withdrawal of the objection.

Claim Objections

Claim 7 is objected to for depending from and including non-elected inventions.

Applicant has rewritten claim 7 in independent form, thereby obviating the objection. As such, Applicant respectfully requests withdrawal of the objection.

Claim Rejections – 35 USC § 102

Claim 7 is rejected under 35 U.S.C. §102(e) as being anticipated by Brenner et al. (US Patent 6,063,906). The Examiner states:

“Brenner et al. teach an antibody that binds SEQ ID NO:24 (see claims 1 and 19). SEQ ID NO:24 is EDEEEEEEEEEEE (12 amino acids long). SEQ ID NO:3 of the instant application has a fragment from amino acid 385-392 and SEQ ID NO:5 from amino acid 243-251 (8 amino acids long) which is identical to the first 8 amino acids of SEQ ID NO:24 of Brenner. Due to the small size of the fragment and high identity with the Brenner peptide, one of ordinary skill in the art would reasonably expect the patented antibody that binds SEQ ID NO:24 of Brenner to

also bind SEQ ID NO:3 or 5 of the instant application in the corresponding region absent evidence to the contrary.”

With this Amendment, Applicant has amended Claim 7 as follows:

“An antibody which binds to an isolated, native SNIP1 polypeptide having the amino acid sequence of SEQ ID Nos: 3 or 5.”

Applicant submits that the antibody recited in the instant claim is not identical to the antibody taught by the cited reference. As acknowledged by the Examiner, Brenner et al., teach an antibody that binds to SEQ ID NO:24, whose sequence is EDEEEEEEEEEEE (12 amino acids long). In contrast, the instant claim is directed to an antibody directed to the 396 and 255 amino acid polypeptides of SEQ ID NO:3 and SEQ ID NO:5, respectively. Applicant acknowledges that there is an eight amino acid overlap between the disclosed polypeptides and the referenced 12mer peptide, and also acknowledges that the cited art teaches an antibody directed to the amino acid sequence EDEEEEEEEEEEE.

Although the cited peptide and subject polypeptide share a common 8 amino acid sequence, the cited antibody directed to the small 12mer peptide is not identical to the claimed antibody directed to polypeptides having lengths of 396 and 255 amino acids.

It is well known that an antibody directed to an epitope of a native polypeptide binds an epitope which is formed by the three-dimensional structure of the native polypeptide. “Regions of a molecule that are recognized specifically by antibodies are called...epitopes. Such sites on *protein surfaces are likely to be composed of amino acids from different parts of the sequence that have been brought together by protein folding.*” (Immunobiology: The Immune System in Health and Disease,” by Janeway & Travers 1997, Elsevier Science Ltd./Garland Publishing, New York, p. 3:9) (emphasis added). As will be appreciated by those of skill in the art, whether or not a particular peptide will act as a good mimic of a protein epitope is highly unpredictable. (See Cheetham et al., (1991) *Proc. Nat’l Acad. Sci. USA* 88:7968-7972). Furthermore, the conformation of an epitope can be affected by amino acid sequence outside of the epitope, as evidenced by Liang et al. (*Arch Biochem Biophys.* (1996) 329:208-14). Liang et al. teach that the binding by an antibody to an epitope of a polypeptide is disrupted when the polypeptide contains C-terminal extended amino acids OUTSIDE the epitope. In view of the teaching of Liang et al. of the influence that the amino acid sequence outside an epitope has on antibody binding, and in view of the significant differences in the amino acid sequence surrounding the 8-

amino acid sequence common to both the cited peptide and the polypeptide disclosed by Applicant, one of skill in the art would expect the epitopes produced by the Brenner peptide (12 amino acids) and the subject polypeptides (396 and 255 amino acids) to have different conformational structures. Thus, the antibodies that recognize and bind to these distinct epitopes would also be different.

Given the differences in epitopes and binding specificities, the Brenner et al. reference does not teach an antibody that binds to an isolated, native SNIP1 polypeptide having the amino acid sequence of SEQ ID NO:3 or SEQ ID NO:5. As discussed above, an antibody against a peptide stretch of a protein will not necessarily bind to the native protein containing the peptide sequence. (See Spangler (1991) *J. Immunol.* 146: 1591-5; Janeway & Travers, *id.*, 3:9). Therefore, in view of the fact that an antibody against a peptide cannot reliably be predicted to recognize a native protein, and in light of the fact that sequences flanking the epitope can have a significant effect on antibody binding, the Brenner et al. reference does not inherently teach an antibody that binds to the isolated, native SNIP1 polypeptides recited in Claim 7. As such, Applicant submits that Claim 7 is novel over the Brenner et al. reference and requests withdrawal of the §102 rejection and reconsideration of amended Claim 7.

Applicant submits that all claims are allowable as written and respectfully request early favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicant's attorney would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney of record.

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Respectfully submitted,



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